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The rising incidence of oesophageal adenocarcinoma in Switzerland

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Introduction

In 2018, an estimated 572,000 oesophageal cancer cases and 509,000 deaths occurred worldwide [1]. In Switzerland, approximately 600 newly diagnosed cases and 460 oesophageal cancer deaths occur each year [2]. Owing to its high lethality, oesophageal cancer has a substantial public health impact in Switzerland and across the world [3, 4].
The main histological types of oesophageal cancer are adenocarcinoma and squamous cell carcinoma. Studies in developed countries have reported substantial rises in the incidence of adenocarcinoma of the oesophagus accompanied by stabilizing or falling rates of oesophageal squamous cell carcinoma [5, 6]. In the US, the incidence of oesophageal adenocarcinoma rose rapidly since the mid-1970s especially among white males, surpassing oesophageal squamous cell carcinoma around the year 1990 [7]. Comparable trends have been observed in several European countries [5, 6]. However, there is substantial variation in both incidence rates and trends between countries and regions most likely driven by differences in risk factors [8]. Adenocarcinoma and squamous cell carcinoma have quite different aetiologies. The key risk factors for oesophageal adenocarcinoma are obesity and gastro-oesophageal reflux disease (GORD) [8],whereas squamous cell carcinomas are mainly related to heavy alcohol consumption, smoking and their synergistic effects [8].

A previous Swiss study covering the period 1982-2011 reported on incidence trends of histological subtypes of oesophageal cancer stratified by language region [9]. However, data for the whole of Switzerland is lacking so far. Therefore, this study evaluated trends in the incidence of oesophageal cancer for both major histologic types in Switzerland using nationally representative data over a 30-year period.

Methods

Data Sources

Data on primary oesophageal cancer cases were extracted from the National Cancer Database managed by the Foundation National Institute for Cancer Epidemiology and Registration (NICER). Population-based cantonal and regional cancer registries collect data directly from the patients' medical records and transmit a defined and pseudonymised subset of the data to NICER. The definition of primary cancers followed the rules as defined by the International Association of Cancer Registries (IACR) and International Association for Research on Cancer (IARC) [10]. The proportion of death certificate only (%DCO) cases and morphologically verified cases (%MV) was 1.7% and 97.3%, respectively. Due to the gradual introduction of cancer registration in Switzerland, population coverage varied from 47.3% in 1986 to 88.3% in 2015.

Cantonal mid-year population estimates for all persons with permanent residence status within each canton were provided by the Swiss Federal Statistical Office.

Classification by histology

Histological categories were classified as: (1) adenocarcinoma (ICD-O-3: M814-M857), (2) squamous cell carcinoma (ICD-O-3: M8050-M8082), (3) other subtypes/NOS (ICD-O-3: M800-M804, M809-M813, M858-M994).

Analytical methods

To assess time trends, annual and 5-year age-standardized incidence rates (ASIR) (direct method, European standard [11]) per 100,000 person-years (PY) were calculated using mid-year population estimates for each canton. Proportions of histological types were calculated based on morphologically confirmed cases. To account for variations in the population coverage of the linguistic regions, we used weights according to the population share ($pop_{linguistic\ region}$ / $pop_{Switzerland}$ per age group, sex and calendar year).

Estimated annual percentage changes (EAPC) with ninety-five percent confidence intervals (95%CI) were obtained by fitting linear regression models using the natural log of annual ASIRs as target variable and the year of incidence as predictor.

Results

Between 1986 and 2015, 9,481 oesophageal cancer cases were diagnosed in the study population (**Tab. 1**). Oesophageal cancer was much more frequent in males than in females resulting in a male-to-female ratio of approximately 3:1. Overall, ASIR of oesophageal cancer slightly increased up to 2001-2005, and stabilised afterwards resulting in an ASIR of 8.3 [95%CI 7.9;8.7] and 2.2 [95%CI 2.0;2.4] per 100,000 PY in 2011-2015 in males and females, respectively.

Between 1986-1990 and 2011-2015, ASIR of oesophageal adenocarcinoma increased significantly in both sexes from 1.4 [95%CI 1.2; 1.7] per 100,000 PY to 4.4 [95%CI 4.1; 4.7] per 100,000 PY in males, and from 0.3 [95%CI 0.2; 0.5] per 100,000 PY to 0.7 [95%CI 0.6; 0.8] per 100,000 PY in females (**Fig. 1**). The increase was slightly steeper in males (EAPC 4.7 [95%CI 3.8; 5.6], p<0.001) compared to females (EAPC 4.5, [95%CI 2.8; 6.3], p<0.001) (**Tab. 1**).

In contrast, incidence of oesophageal squamous cell carcinoma decreased significantly in males by around 1.9% ([95%CI -2.4; -1.4], p<0.001) per year, but remained stable in females (EAPC 0.1, [95%CI -0.6; 0.8], p>0.05). Squamous cell carcinoma was the predominant histologic type during the study period in females. In males, the proportion of oesophageal adenocarcinoma rose substantially from 1986 to 2015 and became the predominant histologic type in males surpassing squamous cell carcinoma in 2006-2010 with a proportion of 50.8% (**Fig. 2**).

Discussion

In the present study, a considerable increase in the occurrence of oesophageal adenocarcinoma was observed in Switzerland, reflecting similar trends in other developed countries [5, 6]. Around the year 2006, oesophageal adenocarcinoma became the predominant histology in the male population, which was previously mainly affected by oesophageal squamous cell carcinoma.

The strong association of tobacco smoking and alcohol consumption with oesophageal squamous cell carcinoma is well documented. In developed countries, these two risk factors account for the biggest proportion of all observed cases (8). In Switzerland, as in other countries in Europe, frequency of smoking-related malignancies [12] and smoking prevalence among males are steadily decreasing [13]. Moreover, alcohol consumption in Switzerland has significantly declined during the last 30 years [14], particularly among men [13]. The important decline in squamous cell carcinoma of the oesophagus in men observed in our study is most likely driven by the falling prevalence of smoking and alcohol consumption. Our results, however, do not show an increasing trend of oesophageal squamous cell carcinoma among Swiss women, despite the rise in smoking prevalence followed in more recent years by a significant increase in both incidence (+50%) and mortality (50%) of lung cancer (1983-1987 to 2008-2012) [12].

	N	EAPC	95% CI	p-value
Males				
Adenocarcinoma	2,617	4.7	[3.8; 5.6]	<0.001
Squamous cell carcinoma	3,956	-1.9	[-2.4; -1.4]	<0.001
Others/NOS	515	-1.1	[-2.5; 0.2]	0.089
Total	7,088	0.4	[-0.1; 0.8]	0.085
Females				
Adenocarcinoma	585	4.5	[2.8; 6.3]	<0.001
Squamous cell carcinoma	1.588	0.1	[-0.6; 0.8]	0.719
Others/NOS	220	-1.1	[-3.1; 1.2]	0.337
Total	2,393	0.9	[0.3; 1.5]	<0.01

Tab. 1.
Estimated annual percentage change for oesophageal cancer by sex and histology from 1986 to 2015.
Others/NOS: other histologic subtype/not otherwise specified.

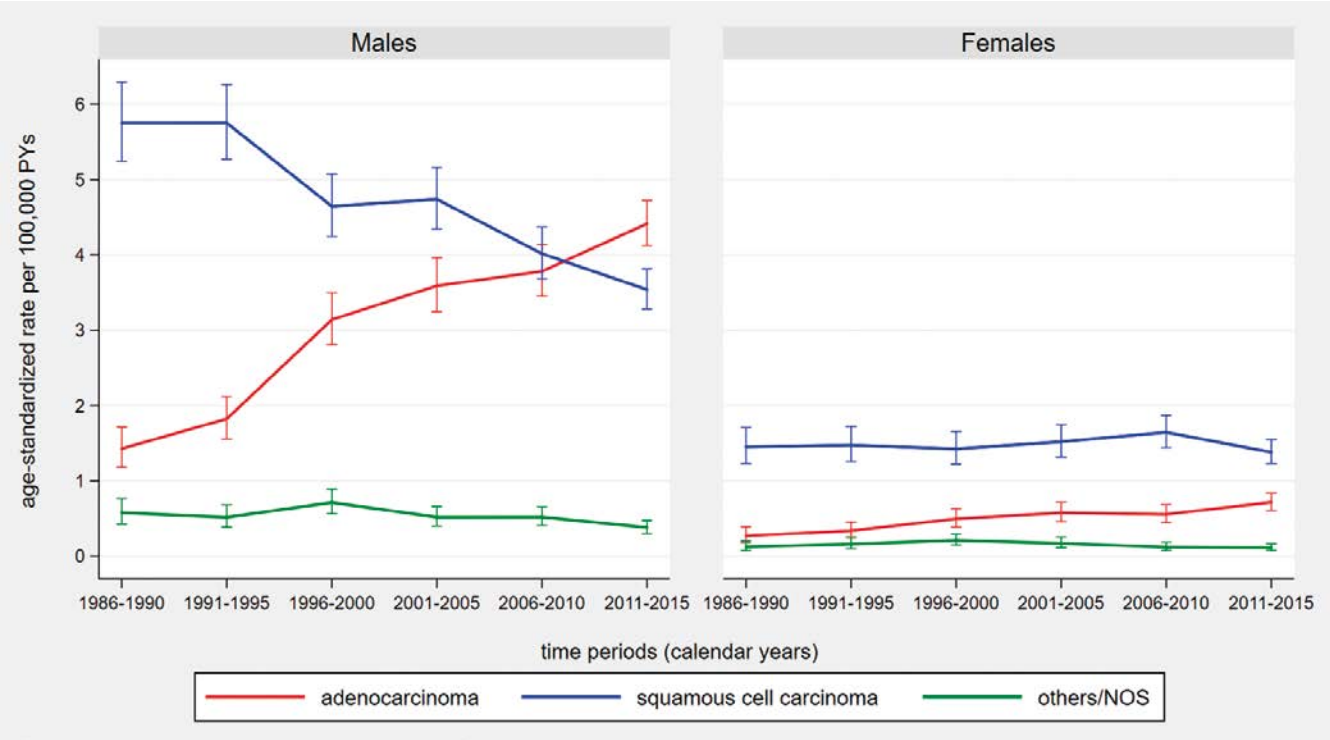

Fig. 1. Time trends in age-standardised incidence rates (European standard population) of oesophageal cancer by sex, histological type, Switzerland 1986-2015. Others/NOS: other histologic subtype/not otherwise specified.

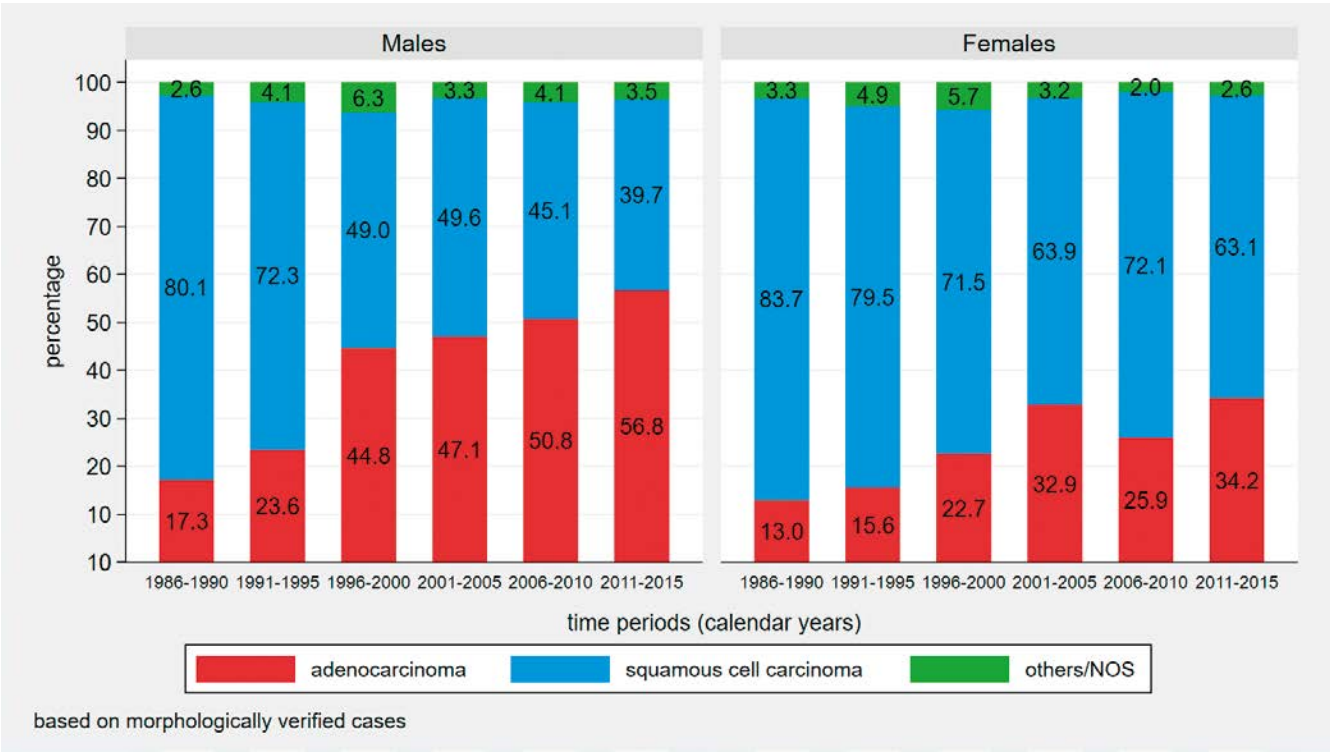

Fig. 2. Time trends in proportions of oesophageal cancer cases by sex, histologic type, Switzerland 1986-2015. Others/NOS: other histologic subtype/not otherwise specified.

Interestingly, a previous Swiss study reported diverging trends in females depending on linguistic region of residence (significantly increasing incidence of oesophageal squamous cell carcinoma in the German-speaking region, stable incidence in the French-Italian-speaking region of Switzerland) [9]. The same study reported lower rates of oesophageal squamous cell carcinoma in males living in the German-speaking region compared to males living in the French-Italian-speaking region of Switzerland, but similar annual percentage decreases [9].

Tobacco smoking is also associated, although less strongly, with an increased occurrence of oesophageal adenocarcinoma [15]. As previously mentioned, smoking prevalence in Swiss males continues to decline. Therefore, smoking seems not to be a major contributing factor for the rising incidence of oesophageal adenocarcinoma in Switzerland. Factors frequently described as being responsible for the rising incidence of oesophageal adenocarcinoma are increasing prevalence of gastro-oesophageal-reflux disease (GORD) and obesity, as well as decreasing prevalence of Helicobacter pylori infections. A strong association between GORD-related symptoms and oesophageal adenocarcinoma was documented. In a 2010 meta-analysis, a 5-fold and 7-fold increase in risk of oesophageal adenocarcinoma was found among individuals reporting, respectively, weekly or daily GORD symptoms, as compared to those with less frequent or no symptoms [16]. In 2004, the prevalence of GORD in the Swiss adult population was 17.6% [17] and was reported to be more frequent in the French-speaking region of Switzerland, but equally distributed among sexes. A meta-analysis established an association between body mass index (BMI) and oesophageal cancer, with an 11% higher likelihood of oesophageal adenocarcinoma occurrence for each 5 kg/m^2 increment of BMI [18]. The International Association of Research on Cancer (IACR) reported a 4.8-fold increased risk of developing oesophageal adenocarcinoma for people falling into the highest BMI category (BMI >=40) compared to normal weighted individuals (BMI 18.5-24.9) [19]. Moreover, BMI likely interacts in synergy with GORD [20]. In recent years, the proportion of overweight and obese individuals has increased, in Switzerland like in other developed countries. Indeed, between 1992 and 2017, the total Swiss overweight population (BMI>=25 kg/m^2) rose from 30% to 42% and in the obese segment (BMI >=30 kg/m^2) from 5% to 11% [13]. Finally, infection by Helicobacter pylori, a known risk factor for non-cardia gastric cancer, appears to be a protective factor against oesophageal adenocarcinoma. A meta-analysis showed that Helicobacter pylori infection confers a nearly 40% lower risk of oesophageal adenocarcinoma [21]. Heuberger et al. investigated the prevalence of Helicobacter pylori infection in Swiss adolescents 1999-2002 and found it to be one of the lowest in Europe (9.7%) [22]. However, it has been questioned whether trends in known risk factors can fully explain the rising incidence and the striking predominance of oesophageal adenocarcinoma in males [23].

Strengths and Weaknesses

This is a Swiss population-based investigation on oesophageal cancer incidence by histological type, which covers a long period of 30 years providing the most representative findings to date. Despite the partial coverage of the Swiss population by the included cancer registries, the important sample size representing the major linguistic regions allows generalizability of our findings to the national level. Moreover, the low proportion of death certificate only cases (2%) indicates a high completeness of case ascertainment.

Uncertainty in distinguishing the organ of origin in cancers occurring at the gastro-oesophageal junction [24] represents an important weakness of our study. In order to deal with this issue, adenocarcinoma of the oesophagus and gastric cardia were combined in the analyses of some other studies. This solution was not an option in our case, because of the high proportion of cases with unspecified anatomical localization. Another limitation of our study is the lack of knowledge on prevalence trends in risk and protective factors covering the whole study period and preceding periods. Finally, our findings may be, at least partially, influenced by improvements in endoscopic technology and an increased standard use of endoscopic procedures resulting in more sensitive detection [25].

Conclusions

A significant increase in the incidence of adenocarcinoma of the oesophagus was observed in Switzerland during the study period 1986-2015. A parallel rise of GORD and obesity over the same period may, at least partially, be responsible for this trend. For oesophageal squamous cell carcinoma, a decreasing trend was only observed in males most likely related to sex-specific lifestyle changes.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: CA Cancer J Clin 68: 394-424, 2018.
2. National Institute for Cancer Epidemiology and Registration (NICER) - Statistics: National Institute for Cancer Epidemiology and Registration (NICER) [03/06/2019]. Available from: http://www.nicer.org/en/statistics-atlas/.
3. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 391: 1023-1075, 2018.

4. Ruhstaller T, Arndt V, Lorez M. Trends in survival from oesophageal cancer in Switzerland Swiss Cancer Bull 3: 227-231, 2014.
5. Arnold M, Laversanne M, Brown LM, et al. Predicting the Future Burden of Esophageal Cancer by Histological Subtype: International Trends in Incidence up to 2030. Am J Gastroenterol 112: 1247-1255, 2017.
6. Wang QL, Xie SH, Wahlin K, Lagergren J. Global time trends in the incidence of esophageal squamous cell carcinoma. Clin Epidemiol 10: 717-728, 2018.
7. Devesa SS, Blot WJ, Fraumeni JF, Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. Cancer 83: 2049-2053, 1998.
8. Torre LA, Siegel RL, Ward EM, Jemal A. Global Cancer Incidence and Mortality Rates and Trends--An Update. Cancer Epidemiol Biomarkers Prev 25: 16-27, 2016.
9. Feller A, Fehr M, Bordoni A, et al. Trends in incidence of oesophageal and gastric cancer according to morphology and anatomical location, in Switzerland 1982-2011. Swiss Med Wkly 145: w14245, 2015.
10. International rules for multiple primary cancers (ICD-O Third Edition). Lyon: International Agency for Research on Cancer (IARC); 2004.
11. Doll R, Cook P. Summarizing indices for comparison of cancer incidence data. Int J Cancer 2: 269-279, 1967.
12. Swiss Cancer Report 2015 - Current situation and developments. Neuchâtel: Federal Statistical Office (FSO), National Institute for Cancer Epidemiology and Registration (NICER), Swiss Childhood Cancer Registry (SCCR); 2016.
13. Schweizerische Gesundheitsbefragung 2017. Neuchâtel: Federal Statistical Office (FSO); 2018.
14. Tackling harmful alcohol use - country note Switzerland: Organisation for Economic Cooperation and Development (OECD); [Available from: http://www.oecd.org/switzerland/Tackling-Harmful-Alcohol-Use-Switzerland-en.pdf.
15. Cook MB, Kamangar F, Whiteman DC, et al. Cigarette smoking and adenocarcinomas of the esophagus and esophagogastric junction: a pooled analysis from the international BEACON consortium. J Natl Cancer Inst 102: 1344-1353, 2010.
16. Rubenstein JH, Taylor JB. Meta-analysis: the association of oesophageal adenocarcinoma with symptoms of gastro-oesophageal reflux. Alimentary Pharmacology & Therapeutics 32: 1222-1227, 2010.
17. Schwenkglenks M, Marbet UA, Szucs TD. Epidemiology and costs of gastroesophageal reflux disease in Switzerland: a population-based study. Sozial- und Praeventivmedizin 49: 51-61, 2004.
18. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol 24: 609-617, 2013.
19. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med 375: 794-798, 2016.
20. Hoyo C, Cook MB, Kamangar F, et al. Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium. Int J Epidemiol 410: 1706-1718, 2012.
21. Xie FJ, Zhang YP, Zheng QQ, et al. Helicobacter pylori infection and esophageal cancer risk: an updated meta-analysis. World J Gastroenterol 19: 6098-6107, 2013.
22. Heuberger F, Pantoflickova D, Gassner M, et al. Helicobacter pylori infection in Swiss adolescents: prevalence and risk factors. Eur J Gastroenterol Hepatol 15: 179-183, 2003.
23. Lagergren J, Lagergren P. Recent developments in esophageal adenocarcinoma. CA Cancer J Clin 63: 232-248, 2013.
24. Pohl H, Welch HG. The role of overdiagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. J Nat Cancer Inst 97: 142-146, 2005.
25. Li-Qing Y. New endoscopic diagnosis and treatment options for early esophageal cancer. J Gastroint Dig Syst, 2012.

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